EXHIBIT C

G2 Inferior Vena Cava Filter: Retrievability and Safety

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PURPOSE: To assess the retrievability of the G2 inferior vena cava (IVC) filter and factors influencing the safety and technical success of retrieval.

MATERIALS AND METHODS: From October 2006 through June 2008, G2 IVC filters were placed in 140 consecutive patients who needed prophylaxis against pulmonary embolism (PE). General indications for filter placement included history of thromboembolic disease (n = 98) and high risk for PE (n = 42); specific indications included contraindication to anticoagulation (n = 120), prophylaxis in addition to anticoagulation (n = 16), and failure of anticoagulation (n = 4). Filter dwell time, technical success of filter retrieval, and complications related to placement or retrieval were retrospectively evaluated in patients who underwent filter removal.

RESULTS: Twenty-seven attempts at G2 filter removal were made in 26 patients (12 men; age range, 24–88 years; mean age, 55.4 y) after a mean period of 122 days (range, 11–260 d). Data were collected retrospectively with institutional review board approval. Filter removal was successful in all 27 attempts (100%). Tilting of the filter (≥15°) occurred in five cases (18.5%), with probable filter incorporation into the right lateral wall of the IVC in one. Other complications of retrieval such as filter thrombosis, significant filter migration, filter fracture, and caval occlusion were not observed.

CONCLUSIONS: G2 IVC filter retrieval has a high technical success rate and a low complication rate. Technical success appears to be unaffected by the dwell time within the reported range.

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Abbreviations: DVT = deep vein thrombosis, IVC = inferior vena cava, PE = pulmonary embolism

THE use of temporary caval interruption is supported by the randomized prospective study by Decousus et al (1), who showed a lower incidence of pulmonary embolism (PE) at 12 days in patients who received a permanent inferior vena cava (IVC) filter and anticoagulation compared with those who received anticoagulation alone. A significantly increased risk of deep vein thrombosis (DVT) at 2 years in the patients who received IVC filters further emphasizes the need for IVC filter retrieval in patients who no longer need the protection. At the time of submission of this study, four optional retrievable (2) IVC filters were commercially available in the United States: the Celect filter (Cook, Bloomington, Indiana), G2 filter (Bard Peripheral Vascular, Tempe, Arizona) Günther Tulip filter (Cook), and OptEase filter (Cordis, Miami Lakes, Florida). The G2 filter is the second generation of the Recovery filter. It has undergone design modifications in attempt to increase resistance to migra-

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tion, improve filter centering within the IVC, and enhance resistance to fracture. The low-profile delivery system, conical shape, and extended retrievability period of the Recovery filter are maintained in the G2 filter. The primary goal of the current study is to evaluate the technical success and complication rates associated with the retrieval of the G2 IVC filter in patients who no longer require inferior vena caval interruption.

MATERIALS AND METHODS

Study Design

One hundred forty consecutive patients underwent placement of a G2 filter at our institution between October 2006 and June 2008. Indications for caval interruption were in accordance with the Society of Interventional Radiology guidelines (2,3). Filters were placed in these patients with the intent of their retrieval after the need for mechanical prophylaxis against PE expired. At our institution, a patient database is kept on all patients who receive a retrievable filter. Information recorded includes the name and medical record of the patient, the name and address of the referring physician, and the date of filter insertion. At 3 months after initial filter placement, a letter is sent to the referring physician, advising filter removal if the patient no longer needs mechanical prophylaxis against PE. Patients are referred to our service for filter retrieval or information is recorded concerning their disposition, such as continuous need for caval interruption or patient death. Another letter is sent at 6 months in the absence of a response. Additional data for this retrospective study were obtained through the Hi-IQ interventional radiology quality assurance database (Conexsys, Woonsocket, Rhode Island).

Of the 140 patients (**Tables 1, 2**), 120 (85.5%) had a contraindication to anticoagulation, 16 (11.3%) required primary prophylaxis in addition to anticoagulation, and four (2.8%) had failure of anticoagulation. Ninety-eight patients (70%) had a history of acute venous thromboembolic disease before filter placement and 42 patients (30%) had no such history but were considered to be at an increased risk for PE. More specifically, 44 patients (32.6%) had a history of acute DVT, 30 (21.3%) had a history of acute PE, 23 (15.6%) had a history of acute DVT and PE, and one (0.7%) had a history of chronic DVT, IVC thrombus, and bilateral renal vein thrombus. Indications for IVC filter placement in the 140 patients included acute DVT and/or PE with or without anticoagulation and/or for prophylaxis against PE (i) in patients with contraindication to anticoagulation, (ii) for primary prophylaxis in addition to anticoagulation, and (iii) in cases of failure of anticoagulation (**Table 2**). Of the 140 patients in whom a G2 filter was placed, 26 met the criteria for filter removal; 12 of these patients were men and 14 were women, with an age range of 24–88 years (mean, 55.4 y). Criteria for filter removal were (i) patient referral to the interventional radiology service by the referring physician, (ii) expired need for PE prophylaxis, (iii) the ability to resume pharmacologic anticoagulation, and (iv) no venographic evidence of significant thrombotic burden associated with the filter immediately before retrieval.

Table 1
Venous Thromboembolic Disease before Filter Placement

Indication	Filter Implantation (N = 140)
History of thromboembolism	
DVT	44 (31.4)
PE	30 (21.4)
DVT and PE	23 (16.4)
DVT/IVC and bilateral renal vein thrombus	1 (0.7)
No history of thromboembolism	42 (30.0)

Note.—Values in parentheses are percentages.

Table 2
Clinical Indications for Filter Placement

Indication	Filter Implantation (N = 140)
Anticoagulation contraindication	120 (85.7)
Primary prophylaxis plus anticoagulation	16 (11.4)
Anticoagulation failure	4 (2.9)

Note.—Values in parentheses are percentages.

Approval and a waiver of consent for this retrospective Health Insurance Portability and Accountability Act–compliant study were granted by our institutional review board. Clinical data for all subjects were obtained from the hospital's electronic medical records and imaging data were retrieved from the picture archiving and communication system (Agfa Impax, Ridgefield Park, New Jersey). Indications for filter implantation, history of venous thromboembolic disease before filter placement, and clinical presentation were recorded for all patients. Images of the retrieval procedures were available for review for 24 of the 26 patients (27 procedures). Two G2 IVC filters were placed and retrieved in a single patient over the course of the study, with a total implantation time of 193 days. The degree of filter tilting was measured by the angle formed and measured between the orientation of the long axis of the filter and that of the IVC. Filter tilting data could not be evaluated in two patients.

Device

The G2 IVC filter is so titled as it represents the second generation of the Recovery filter (Bard Peripheral Vascular), which is no longer commercially available in the United States. The former is composed of twelve 0.013-inch nitinol wires that join at the apex of the filter. Six of these wires measure 19.8 mm in length and form the arms. The remaining six wires have anchoring hooks at their tips and form the legs. The resting leg span is 40 mm, with a filter measuring 40 mm in height (4). As for the Recovery filter, maximum recommended IVC diameter for G2 filter placement remains 2.8 cm.

Insertion Technique

Sterile technique and fluoroscopic guidance were used for all filter insertion procedures. Venous access was gained to the right common femoral vein with palpation and Seldinger techniques or one-wall venous entry with use of a 5-F micropuncture kit (B. Braun, Bethlehem, Pennsylvania). When the right jugular vein was used, access was gained with sonographic guidance and

the micropuncture set. An inferior vena cavogram would then be obtained with use of a 5-F straight flush catheter (Angiodynamics, Queensbury, New York), with the distal tip left within the distal left common iliac vein or at the right and left iliac vein confluence. All filters were placed within the infrarenal segment of the IVC. The authors do not place G2 filters as recommended for all other filters, at approximately 1 cm inferior to the most inferior renal vein. Instead, G2 filters are placed more than 1 cm inferior to the most inferior renal vein. Anecdotal experience with the placement and retrieval of the Recovery filter had shown a not-uncommon migration of one or two filter arms into a renal vein. This would not present immediately after filter deployment but would be noted immediately before the retrieval procedure.

Filters were placed with use of the 7-F femoral or 10-F jugular G2 introducer and dilator set. After filter advancement within the delivery sheath to the desired location within the IVC, the filter is typically unsheathed and deployed by retraction of the delivery sheath while the pusher wire is kept stationary.

Retrieval Procedure

All procedures were performed with the patient receiving local anesthesia or conscious sedation via a right internal jugular vein approach. After standard preparation of the access site, the vein is accessed with a 21-gauge needle with sonographic guidance. A 5-F micropuncture set (B. Braun) is then used to accommodate the insertion of an 0.035-inch Bentson wire (Angiodynamics) with fluoroscopic guidance. Over this wire, a 5-F, 100-cm Berenstein catheter (Cook) is inserted, with the distal tip advanced into the IVC. A 0.035-inch Glidewire (Terumo, Somerset, New Jersey) is then used to negotiate through the filter, with the distal tip of the angled catheter rested within the proximal IVC or left common iliac vein. Great effort is made to traverse the filter on the "short" side, where the filter (ie, superior tip) head has the shortest distance to the adjacent caval wall. This true route is confirmed by the demonstration of gentle filter movement, ie, "straightening" deviation of the filter superior cone by the catheter. Originally described by Asch (5), this allows for the centering of the filter head within the IVC lumen, simplifying its retrieval.

After satisfactory advancement and placement of the catheter through the indwelling filter, an inferior vena cavogram is obtained with use of iodinated contrast medium.

After confirmation of the absence of thrombus or lack of significant trapped thrombus within the filter, the angiographic catheter is exchanged over a 260-cm Amplatz wire (Cook) for a 12-F introducer sheath. Over the wire and through this sheath, a 10-F Recovery Cone retrieval system (Bard Peripheral Vascular) is advanced, with the distal tip advanced to the superior aspect of the indwelling filter head. With the wire in place, the Recovery cone is then used to negotiate and catch the head of the filter. The sheath is advanced over the filter, collapsing it within its lumen. The filter is then retracted into the catheter and out of the patient's venous system. A repeat inferior vena cavogram is obtained to evaluate the integrity of the IVC, especially at the segment where the filter was housed.

Study Endpoints

The primary endpoint of the study was successful retrieval of the filter. Various associated parameters were measured: filter retrieval success rate, mean implantation time, filter tilting, and migration. Filter tilting of more than 15° from the long axis of the IVC is considered substantial (4). Migration is defined as a change in cephalocaudal position of greater than 2 cm. Other parameters reviewed were thrombus associated with the filter, strut fracture, and caval stenosis.

RESULTS

Filter Insertion

All patients had successful placement of their filter in the infrarenal IVC, without complications. Of the 26 patients who had their filters retrieved, 14 (54%) had their filters inserted from the right common femoral vein approach and 12 (46%) had their filters inserted from the right internal jugular vein.

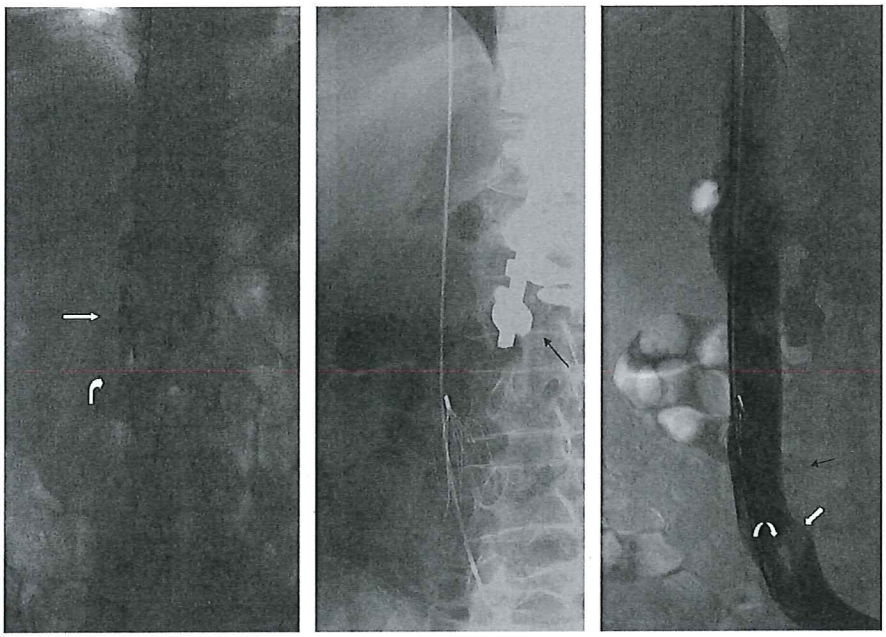
Retrieval Procedure

Among the 140 patients who had G2 IVC filters placed, 26 were referred for filter retrieval. All retrieval procedures were performed via the right internal jugular approach. All 26 patients had successful G2 filter retrieval, resulting in a technical success rate of 100%. The mean interval between filter implantation and retrieval was 122 days (range, 11–260 d). One patient had placement and retrieval of two G2 filters over the course of the study, with a mean implantation time of 193 days. Tilting of the filter (>15°) occurred in five patients (18.5%), with a maximum of 28° of tilt from the long axis of the IVC. The filter was successfully removed in all these patients. No significant cephalad or caudal migration of the filter was identified in any of the patients. One patient had caudal migration of less than 2 cm (or approximately half of a vertebral body height), as illustrated in **Figure 1**. This may have contributed to the progressive tilting of the filter. No angiographic demonstration of thrombus was found to be associated with the filter in any of the study patients. No strut fracture was demonstrated in vivo and on retrieval of the filters. Minimal segmental IVC irregularity was present after filter retrieval in all patients. No significant caval stenosis or penetration was shown on the completion inferior vena cavograms.

DISCUSSION

Although there was no venographic demonstration of thrombus associated with any of the indwelling filters, small linear strands were found to be associated with the majority of the retrieved filters. The retrieved tissues were not sent for laboratory analysis for further characterization. These are presumed to be thrombotic in nature. It is uncertain whether these thrombi formed at the time of filter retrieval or were present in vivo and venographically silent.

Procedure times were not recorded during the procedures and could not be reported in this retrospective study. We could not determine the degree to which filter tilting affects procedure times. It is intuitive to believe that procedural time would be directly proportional to the degree of filter tilt. This may be proven in future prospective studies.



a. b. c.

Figure 1. Progression of filter tilt. **(a)** Frontal image immediately after G2 filter (bent arrow) deployment shows minimal tilting (venographic image not shown). Note the distal tip of the delivery sheath and inner pusher (straight arrow) immediately superior to the filter. **(b)** Image obtained 7 months after initial deployment shows further tilting immediately before filter retrieval. Note the new spinal fixation hardware (arrow). **(c)** The filter apex was centered (not shown) with the angiographic catheter advanced toward the side of filter tilt. Incidental note is made of two filter struts (black arrow) projecting beyond the contour of the medial caval wall. Note is also made of partial duplication of the left common iliac vein versus endoluminal web formation (straight block arrow), associated with the tubular extrinsic compression by the crossing right common iliac artery (straight white arrow).

Table 3
Retrieval Results

Characteristic	Filter Retrieval (n = 27)
Mean age ± SD (y)	56 ± 18.8
Female sex	14 (51.9)
Mean dwell time (d)	
Mean	122
Range	11–260
Tilt (°)	
Mean	10
Range	5–28

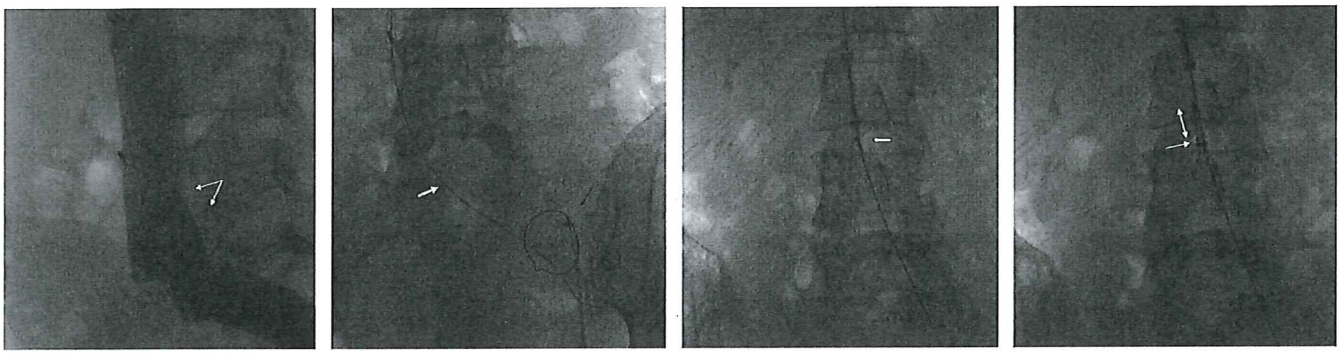
Note.—Values in parentheses are percentages.

Table 4
Filter Tilting

Tilt (°)	Immediately after Placement (n = 27)	Immediately before Retrieval (n = 24)
<5–9	13	12
10–14	1	6
>15	2	5
Unknown	11	1

As illustrated in **Tables 3** and **4**, in this study, the mean filter tilt is 10°, with a range from less than 5° to 28°. Filter tilting of greater than 15° is considered significant by many investigators (10–12). Filter tilting has implications on the risk of new PE and recurrent PE with a caval filter in place. Tilting of conical IVC filters has been associated with recurrent PE (10,13). This did not occur in our patient study cohort. In the series reported by Rogers et al (14), with a 5-year follow-up period, patients with filters tilting more than 14° experienced a significantly higher incidence of recurrent PE. Of note, in the present study, images obtained immediately after filter deployment and immediately before filter retrieval were available for review in 24 patients. Limitations of these data include the unavailability of images obtained after filter deployment to review for 11 patients. This is mainly because of our institution's transition to a picture archiving and communication system during the course of the study period, in addition to the lack of film printing before this transition. Among the 24 patients whose images before filter retrieval were available for review, five filters (21%) had a tilt angle greater than 15°. Among the 15 patients with both sets of procedural images available for review, two filters (13%) showed a tilting progression from less than 5° to greater than 15° (**Fig. 1**); two other patients (13%) had tilting progression from 15° to 20° and from 20° to 28°; and two (13%) had regression of the filter tilting angle from greater than 15° to less than 5°. Hence, there is some relative tilt angle instability of the G2 filters while in place. However, this did not affect their retrieval. A 43-year-old woman with PE had a G2 filter placed to prevent further embolic events from a right popliteal vein thrombus. With the continuation of anticoagulation, she was referred for filter retrieval 121 days after initial placement. Sonographic evaluation of the lower extremities showed no current DVT. Comparison of the venographic images revealed progression of filter tilting, from 20° to 28° (**Fig 2**), with the filter's apical cone apposed to the lateral caval wall. Attempt to center the apical filter cone with a properly positioned guide wire was not successful. A snare wire was then advanced, through a 6-F introducer sheath, via the left common femoral vein. This was used to apply gentle traction to the guide wire traversing the filter, with resultant centering of the apex. This then led to its successful retrieval by the Recovery Cone.

In this study, 100% of the G2 filters intended for retrieval were successfully retrieved. Of the 140 patients in whom a G2 filter was placed, 26 (19%) had the filter removed. In the retrospective study by Grande et al (6), 13% of the patients had their filter removed. Oliva et al (4) reported 51 filter retrievals in a prospective study group of 120 patients. In our study, most retrieval procedures were simple and short in duration. However, the procedure was complicated by signifi-



a. b. c. d.

Figure 2. Filter retrieval with adjunct advanced maneuvers. **(a)** Significant tilting of the indwelling filter is noted before attempted retrieval. In addition, two filter struts (arrows) project beyond the contour of the posteromedial wall of the proximal IVC, suggestive of wall penetration. **(b)** A stiff guide wire (white arrow) properly positioned toward the side of filter tilt failed to center the filter apex. Further wire force is generated by gentle traction of a loop snare wire (black arrow) inserted from the left common femoral vein. **(c)** Traction of the guide wire with the loop snare wire (not shown) appears successful in centering the filter cone (arrow). **(d)** With the filter apex centered, it was successfully caught by the Recovery Cone. Here, the G2 filter appears partly within the sheath (tip shown by horizontal arrow; shaft shown by vertical arrowheads) immediately before complete retrieval.

cant filter tilting, for which further filter manipulations were necessary to accommodate successful retrieval. Catheter and wire manipulations of the filter mainly aim to center the apical cone of the filter for easier snaring by the Recovery Cone system. Guide and tip-deflecting wires and snares have been used with relative success in straightening tilted filters (6–9).

It is our belief that multiplanar imaging (eg, computed tomography [CT] or magnetic resonance imaging) is the best method to ascertain filter penetration of the caval wall. The projection of filter struts beyond the caval wall on venography may not be sufficient to confirm their penetration, as some of these struts may simply be indenting the venous wall to a variable degree. The majority of the patients did not undergo an abdominal CT scan during the course of this study. For this reason, we could not determine and do not report the percentage of filter caval penetration in this study.

During inferior vena cavography before retrieval, no patient exhibited any significant endoluminal thrombus associated with the indwelling G2 filter, and all patients presenting for retrieval had successful filter retrieval. This was found to be surprising given the natural history of indwelling filters. With a mean filter implantation time of 53.4 days, Oliva et al (4) recently reported a large amount of trapped thrombi within the indwelling G2 filter in eight of 59 patients (13.6%). These patients did not have their filters removed. The very low rate of filter thrombosis in our study may be related to the patient population. As shown in **Table 5**, a plurality of this patient cohort (42%) had no DVT or PE and filter insertion was for prophylaxis during projected prolonged bed rest after an orthopedic surgical procedure. In this small study, no patient had symptomatic PE.

Table 5
Clinical Indications for Filter Placement in Patients Whose Filters Were Retrieved

Indication	Filter Implantation (n = 26)
No history of thromboembolic disease	
DVT and preoperative state	2 (8)
DVT and PE	3 (12)
PE only	3 (12)
Primary prophylaxis	11 (42)
History of thromboembolic disease	
PE only	3 (12)
DVT and prophylaxis	2 (8)
DVT and PE	1 (4)

Note.—Values in parentheses are percentages rounded off to the nearest whole number.

There were no major complications in any of the patients in this study. A minority of the patients had pain during the retrieval procedure. However, vague intraprocedural abdominal pain was limited to the period of time when the filter was collapsed and pulled into the Recovery Cone. Pain quickly dissipated immediately after successful retrieval of the filter into the Recovery Cone sheath. The retrospective nature of this study does not afford any further quantification of this minor complication. The majority of the patients received intravenous sedation with midazolam and fentanyl during the procedure.

There are limitations to this study, the primary one being its retrospective nature. The focus was mainly to assess the technical success of filter retrieval and to evaluate any related complications. There was no systematic follow-up of patients who underwent the placement of a G2 filter. In this report, the mean and longest filter dwell times, 122 and 260 days, respectively, do not afford proper evaluation of the G2 filter as a permanent device. Of particular interest, the long-term risk of caval thrombosis after G2 filter placement cannot be assessed. The small number of patients in our study is insufficient to make any broad conclusions except to affirm the high retrieval and low procedure complication rates associated with the G2 filter. The number of patients also does not afford full assessment of the significance of filter tilting and its effect on filter efficacy and filter retrieval proce-

dure time. Filter migration and positional stability could not be evaluated in all patients in this study because of the inability to compare venographic images, as these were not available in all patients from the time of initial filter deployment (as described earlier).

The value of this study is to supplement and confirm the results previously reported by Oliva et al (4). The patient cohort in our study is smaller, but confirmation of single-center results with those of another institution is of value.

In summary, there is a high technical success rate associated with the retrieval of the G2 filter. This does not appear to be limited by filter tilting within the reported range in this small study group. In addition, there appears to be a very low complication rate. In the short term, it appears that the G2 filter is associated with a very low rate of thrombosis, a very low rate of symptomatic PE, a very high retrieval technical success rate, and a good retrieval safety profile.

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